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EXAMINER	
SANG, HONG	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,168	TERNESS ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7 and 11-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Terness et al.

1. Applicant's election with traverse of Group I (claims 1-6 and 8-10), and species election of SEQ ID NO.1 and melanoma in the reply filed on 10/22/07 is acknowledged. The traversal is on the ground(s) that the groups designated by the examiner fail to define compositions with properties so distinct as to warrant separate examination and search, and searching all the groups together would not present an undue burden. Moreover, Groups I and V are not different inventions, since they are merely directed to a surface protein and an antibody to the same. This is not found persuasive because the instant case is a national stage filing of an international application (i.e. 35 U.S.C. 371) and therefore the standard of burdensome search is not applied. As indicated in the last office action, the special technique feature liking the claimed inventions is known in the art, and as such unity of the invention is lacking (see office action mailed on 4/19/07, page 3). Therefore, the separation of claims into different groups was deemed proper, and therefore made FINAL.

2. Claims 1-24 are pending. Claims 7 and 11-24 are withdrawn from further consideration as being drawn to non-elected inventions.

3. Claims 1-6 and 8-10 are under examination.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

5. The information disclosure statement (IDS) filed on 6/3/05 has been considered. A signed copy is attached hereto.

Specification

6. The disclosure is objected to because of the following informality.

The Brief Description of the Drawings does not reference each of the Figures. The Brief Description should be amended to reference Figures 17A, 17B, 18A, 18B, 21A, 21B, 22A, 22B, 23A, and 23B.

The Brief Description for Figure 19c mentions (a) and (b), which are not found in Figure 19c.

The Brief Description for Figure 27 describes (a), (b), (c) and (d), however, only (a), (b) and (c) are found in Figure 27.

The Brief Description for Figure 29ef describes (d) and (e) instead of (e) and (f).

Appropriate correction is required.

Claim Objections

7. Claims 2, 3, and 8 are objected to because of the following informalities:

A. Claim 2 is objected to for reciting the term "other cells". It is unclear what cells the term refers to. Does it refer to any cells or some specific cells?

B. Claim 3 recites "isolating the gel band of the protein". It is unclear which gel band (i.e. at what molecular weight) is to be isolated. One skilled in the art would

expect many bands on the gel because the protein preparation isolated from human blood cell membrane contains a mixture of proteins.

C. Claim 8 is objected to because it depends from a non-elected claim (i.e. claim 7). Appropriate correction is required.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1-5 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter

Claims 1-5, as written, do not sufficiently distinguish over glycoproteins as they exists naturally because claims do not particularly point out any non-naturally occurring differences between the claimed glycoproteins and the naturally occurring glycoproteins.

In the absence of the hand of man, the naturally occurring glycoproteins are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" glycoprotein or similar language would obviate this rejection.

Although claims 3 and 4 recite the phrase "obtainable from human blood by (a) isolating and lysing cells;" the word "obtainable" does not limit the glycoproteins to those that are obtained by the recited process. Therefore claims 3 and 4 still read on the naturally occurring glycoprotein.

Claim Rejections - 35 USC § 112, 2nd paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite for reciting the phrase "functional derivative or active fraction thereof" as the exact meaning of the phrase is not known. The term "derivative" is not one, which has a universally accepted meaning in the art nor is it one which has been adequately described in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. Since it is unclear how the ACA protein is to be derivatized to yield the class of molecules referred to in the claims, a person of skill in the art cannot ascribe a discrete and identifiable class of molecules to said phrase. Moreover, it is unclear what function and activity the phrase refers to. Is it an enzymatic function or activity, or a characteristic such as overexpression in tumor cells? Aside from the expression in different cells, the

specification does not disclose any biological function or activity for the disclosed ACA polypeptide.

Claim Rejections - 35 USC § 112, 1st paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 2-6 and 8-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is made because: i) applicants are claiming a genus of molecules having part or all characteristics recited in the claims, as well as functional derivative, and active fraction thereof while the specification only describes one ACA glycoprotein; ii) applicants are claiming a recombinant protein while the specification only discloses a partial amino acid sequence for the protein (details see following discussion).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical

and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Claims 2-6, and 9-10 are depend from claim 1. Claim 1 is drawn to a surface glycoprotein comprising the following features: (a) it is GPI-anchored on the cell surface; (b) it can be removed from the cell membrane by treatment with PI-PLC; and (c) its GPI-anchor is characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor. Claims 2 is drawn to the surface glycoprotein of claim 1, which is the surface glycoprotein ACA characterized by the following additional features: (d) it has an isoelectric point of pH 5.5; (e) it is present on progenitor cells, granulocytes, monocytes, B-cells (but not T-cells), melanocytes, and other cells; (f) it is preferentially expressed during cell division and in tumor cells, or functional derivative or active fraction thereof. Claims 3-5 and 9-10 are drawn to the surface glycoprotein ACA of claim 2, wherein the surface glycoprotein ACA is isolated from human blood, has a molecular weight of 65 or 68 kD when analyzed by SDS PAGE under reducing conditions, contains at least one of the sequences selected from SEQ ID NO.1-11, or is a recombinant protein produced in a mammalian cell.

Claim 8 is drawn to a surface glycoprotein ACA that is obtained from human blood and characterized by the molecular weight of 65 or 68 kD.

Claim 1 is drawn to a genus of GPI-anchored protein having the recited characteristics. A person of skilled in the art could readily envision all the GPI-anchored proteins since the GPI-anchored proteins having the recited characteristics are well-known in the art. One of ordinary skill in the art would conclude that applicant was in possession of the genus based on the general knowledge in the art. Clams 2-6, and 8-10 are drawn to a subgenus of the GPI-anchored protein that having additional features such as the specific isoelectric point, obtained from blood, molecular weight and partial sequences. The subgenus encompasses any and all surface glycoproteins (which include those yet to be discovered), and fragments, derivatives thereof that have part or all characteristics recited in the claims. The specification in this case discloses only one species (one member) within the subgenus, i.e. the surface glycoprotein ACA that is characterized by all the features recited in the claims, i.e. (a) it is GPI-anchored on the cell surface; (b) it can be removed from the cell membrane by treatment with PI-PLC; (c) its GPI-anchor is characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor; (d) it has an isoelectric point of pH 5.5; (e) it is present on progenitor cells, granulocytes, monocytes, B-cells (but not T-cells), melanocytes, and other cells; (f) it is preferentially expressed during cell division and in tumor cells; (g) it has a molecular weight of 65 or 68 kD when analyzed by SDS PAGE under reducing conditions, and (h) it contains all the amino acid sequences SEQ ID NO.1-11. The specification does not disclose any protein that only has part of the features recited in the claims. For example, the specification does not disclose a glycoprotein protein having isoelectric point of 5.5, and a molecular weight different from 65 or 68 kD. The

specification does not disclose a protein comprising only one, but not other sequences selected from SEQ ID NOs.1-11. The specification does not disclose any biological function or activity of the disclosed ACA protein except the features recited in claims 2-6, and 8-10. The specification does not show any proteins having part of the features recited in the claims, in fact have the same function of the disclosed single surface glycoprotein ACA. The general knowledge in the art does not provide any indication of how the structure of one glycoprotein having the recited characteristics (e.g. obtained from human blood and has molecular weight 6.5 or 6.8, see claim 8) is representative of unknown glycoprotein having the same characteristics. The nature of the GPI anchored proteins is that they have variant structures, and in the present state of the art the structures of one does not provide guidance to the structure of others. Low (Biochim. Biophys. Acta, 1989, 988:427-454) states that proteins with GPI anchor have been identified in organisms as diverse as mammals, insects, protozoa, yeast, and slime modes; the majority of these proteins are located on the cell surface, and where studied, all are believed to utilize the C-terminal amino acid of the polypeptide for membrane anchoring; apart from these, the proteins show no obvious similarities (see page 428, 2nd column, 3rd paragraph). Low teaches that there are no similarities at the amino sequence level although several of these proteins have been assigned to the immunoglobulin gene superfamily (see page 428, 2nd column, 3rd paragraph). Low teaches that in addition to the structural diversity described above, the protein exhibit large differences in biochemical function (see page 428, 2nd column, 4th paragraph). Low teaches that the largest single grouping is enzyme, and they vary substantially in

their substrates (see page 428, 2nd column, 3rd paragraph). In the instant case, applicants are claiming a genus of glycoproteins including those yet to be discovered, however, the common structure attributes of the genus are not described in the instant specification. While claims limit the glycoproteins to those having the specific features recited in the claims, the specification does not disclose how these features are correlated to the structures. In the absence of structural characteristics that are shared by members of the genus, one of skill in the art would reasonably conclude that applicant was not in possession of the claimed genus because description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

With regard to the functional derivatives and active fragments, applicant does not appear to have reduced to practice any biological derivative or active fragment of an ACA glycoprotein. Neither has applicant provided sufficient descriptive information such as definitive structural features that are common to the genus of derivatives or active fragments. That is, the specification provides neither a representative number of the derivatives or active fragments, nor does it provide a descriptive of structural features that are common to the derivatives and active fragments. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a single species is insufficient to describe a highly variant genus. Because the genus of molecules is extensive and the artisan cannot envision the detailed structure of the encompassed glycoproteins, derivatives and active fragments and therefore conception is not achieved until

reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Thus one of skill in the art would not be able to recognize that applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Therefore, only the ACA protein have all the features recited in claims 2-5 (GPI anchored, obtained from human blood, isoelectric point, molecular weight, comprising SEQ ID NO.1-11), but not the full breadth of a surface glycoprotein ACA, functional derivatives, and active fragments thereof meet the written description provision of 35 U.S.C. § 112 first paragraph.

Applicants are not in possession of the claimed recombinant protein. Claims 8 and 9 are drawn to a recombinant protein of a surface glycoprotein ACA, for which they provided only partial sequence. In order to make a recombinant protein, one would need to have the sequence of the DNA encoding the protein. The court stated "since

applicants claimed nucleic acids encoding protein for which they provided only partial sequence, and without approximately 95 percent of amino acid sequence that applicants did not disclose, it cannot be held that DNA molecules claimed in application have been described, since applicant's contention that they were in physical possession of protein does not establish their knowledge of that protein's amino acid sequence or any of its other descriptive properties." *See in re Wallach 71 USPQ2d 1939 (Fed. Cir. 2004).* The court stated "Given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met". In the instant case, applicants have not provided any evidence that the full amino acid sequence of a protein can be deduced from a partial sequence and the limited additional physical characteristics that they have identified. Without the full sequence, one skilled in the art would not conclude that applicants are in possession of the DNA encoding the protein, and as such applicants are not in possession of the recombinant protein.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 112, 1st paragraph

14. Claims 2-6 and 8-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the surface glycoprotein ACA, a salt thereof that is characterized by all the features recited in claims 2-6 and 8-10, i.e. (a) it is GPI-anchored on the cell surface; (b) it can be removed from the cell membrane by treatment with PI-PLC; (c) its GPI-anchor is characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor; (d) it has an isoelectric point of pH 5.5; (e) it is present on progenitor cells, granulocytes, monocytes, B-cells (but not T-cells), melanocytes, and other cells; (f) it is preferentially expressed during cell division and in tumor cells; (g) it has a molecular weight of 65 or 68 kD when analyzed by SDS PAGE under reducing conditions, and (h) it contains the amino acid sequences SEQ ID NO.1-11, does not reasonably provide enablement for any and all surface glycoprotein ACA, functional derivatives, active fragments, and recombinant proteins thereof that is characterized by the features disclosed in claims 2-5 and 8-10,. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Claims 2-6, and 9-10 are drawn to a surface glycoprotein ACA, a salt, a functional derivatives, an active fragments thereof that is characterized by the following features, i.e. (a) it is GPI-anchored on the cell surface; (b) it can be removed from the cell membrane by treatment with PI-PLC; (c) its GPI-anchor is characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor; (d) it has an isoelectric point of pH 5.5; (e) it is present on progenitor cells, granulocytes, monocytes, B-cells (but not T-cells), melanocytes, and other cells; (f) it is preferentially expressed during cell division and in tumor cells. Claims are further limited wherein the surface glycoprotein is obtained from blood, having a molecular weight of 65 or 68 kD when analyzed by SDS PAGE under reducing conditions, or contains at least one of the following amino acid sequence selected from the group consisting of SEQ ID NO.1-11, is a recombinant protein which is produced in a mammalian cell.

Claim 8 is drawn to a surface glycoprotein ACA isolated from human blood, and having a molecular weight of 65 or 68 kD.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

Applicants are claiming a genus of molecules including any and all ACA glycoproteins having part or all of the features recited in the claims, functional derivatives, active fragments, recombinant protein thereof. Therefore, the breadth of the claims is extremely broad.

Quantity of experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the structure and function of the claimed surface glycoproteins, functional derivatives and active fragments thereof. Moreover, it would require undue experimentation to determine which of the surface glycoproteins, functional derivatives, and active fragments thereof are in fact having the same function as the disclosed single ACA protein, e.g. capable of diagnosing cancer. The identification and characterization of each of these surface glycoproteins, functional derivatives, and active fragments would be inventive, unpredictable, and difficult in itself, requiring years of inventive effort with no guarantee of success in doing so.

One cannot extrapolate the teachings of the specification to the scope of the claims because the specification only teaches a single GPI-anchored surface

glycoprotein ACA, which comprises all SEQ ID NOS.1-11, has isoelectric point of 5.5 and molecular weight of 65 or 68 kD, and the claims are broadly drawn to any and all GPI anchored proteins having part of the features recited in the claims, functional derivatives, and active fragments thereof, and applicant has not enabled all of these types of molecules because it has not been shown that these molecules are capable of functioning as the disclosed ACA glycoprotein.

The state of the prior art and the predictability or lack thereof in the art:

Protein chemistry is probably one of the most unpredictable areas of biotechnology. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the

biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make all the surface glycoproteins, active fragments, functional derivatives thereof that have the recited features.

Working examples:

The specification teaches purification and isolation of one surface glycoprotein ACA having all the features recited in the claims from human red blood cell (erythrocyte) membranes (see Example 1). The specification teaches partial sequences (i.e. SEQ ID

NO.11) of the protein obtained by sequencing the 11 tryptic peptides (see Example 2). The specification discloses detection of the ACA protein in different types of cells (see Examples 7, and 9-13). The specification teaches that O- and N-glycosylation leads to different molecular mass forms of human glycoprotein ACA (i.e. the observed 65 and 68 kD) (see Example 14). The specification does not teach any other surface glycoprotein. The specification does not teach any functional derivative, and active fragment of the ACA.

Guidance in the specification

Applicants claim a genus of surface glycoproteins, functional derivatives and active fragments thereof with the characteristics recited in the claims. However, the specification does not teach how to make such broad class of molecules. Furthermore, it is not clear what criteria would be used to make the functional derivatives and active fragments. Moreover, it is unclear what function and activity it is referred to. Without such guidance, the changes which can be made in the protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

With regard to claim 8, although one skilled in the art could obtain all the membrane glycoproteins from human blood that have the molecular weight 65 or 68 kD, one would not know how to use all these proteins. The proteins having the molecular weight of 65 or 68 kD that is isolated from erythrocytes may be structurally and functionally distinct from the one that is isolated from different blood cells. For example,

Harada et al. (Glycoconjugate J. 1992, 9: 198-203) teach a surface glycoprotein that is isolated from human natural killer cells and has molecular weight of 65 kD as determined by SDS-PAGE gel under reducing condition (see abstract, and page 199, 1st column, 3rd paragraph). However, this protein has different isoelectric point (4.1-4.6), indicating the structure of this protein is different from the instant ACA glycoprotein. Therefore, one skilled in the art would recognize that proteins having same molecular weight but isolated from different blood cells may not have the same function.

Moreover, applicants have not provided any evidence that the full amino acid sequence of a protein can be deduced from a partial sequence and the limited additional physical characteristics that they have identified. Without the full sequence, one skilled in the art would not conclude that applicants are able to make the recombinant protein.

Level of skill in the art

The level of the skill in the art is deemed to be high

Conclusion:

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example which teaches functional derivative, active fragments of the surface glycoprotein ACA, and all other undisclosed glycoproteins, and the negative

teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,519,120 (Date of Patent: 5/21/1996), as evidenced by Chen et al. (PNAS 1998, 95: 9512-9517, IDS).

US 5,519,120 (Date of Patent: 5/21/1996) teaches a GPI-anchored protein μ-PAR which can be removed from the cell surface by treatment with PI-PLC (see columns 55-56). US 5,519,120 teaches that the majority of the GPI-anchored proteins are susceptible to PI-PLC, which releases the proteins into the medium by removing the diacylglycerol portion of the glycolipid (see column 55, lines 54-60). Because μ-PAR can be removed by the treatment of PI-PLC, its GPI-anchor would have a non-acetylated inositol ring as evidenced by Chen et al. Chen et al. teach that the PI-PLC resistance of a GPI-anchored protein is due to acetylation of an inositol hydroxyl group (see page 9512, left column, last paragraph). Moreover, US 5,519,120 teaches treating cells with PI-PLC (see column 55-56), the proteins, which are released into the medium by PI-

PLC treatment, include all the GPI-anchored proteins that are present on the cell surface. Such GPI-anchored proteins would include those that are characterized by a non-acetylated inositol ring and diacyl glycerol as lipid tail of the anchor. Therefore, US 5,519,120 teaches all the limitations of claim 1.

US 5,519,120 teaches that the μ-PAR was originally identified in blood monocytes (see column 3, lines 421-43). US 5,519,120 teaches that the molecular weight of μ-PAR detected by SDS-PAGE under reducing condition using an antibody is about 67 kD (covering 65-68 Kd region, see Figures 4A and 5A, and column 47, line 43). Claim 8 is a product by process claims.

MPEP 2113 [R-1] states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). MPEP further states "The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

In the instant case, the product μ-PAR of the prior art appears to be the same as the product of claim 8 because they both are isolated from blood cells and have the same molecular weight. Moreover, the claims do not define that manufacturing process steps impart any distinctive structural characteristics to the final product compared to the product in the prior art, the patentability of the product cited in claim 8 does not depend on its method of production.

17. Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Harada et al. (Glycoconj. J. 1992, Aug., 9(4): 198-203).

Harada et al. teach a surface glycoprotein that is isolated from human blood cells i.e. natural killer cells and has molecular weight of 65 kD as determined by SDS-PAGE gel under reducing condition (see abstract, and page 199, 1st column, 3rd paragraph).

Claim 8 is a product by process claims.

MPEP 2113 [R-1] states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). MPEP further states "The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the

product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

In the instant case, the surface glycoprotein disclosed by Harada et al. appears to be the same as the product of claim 8 because they both are isolated from blood cells and have the same molecular weight. Moreover, the claims do not define that manufacturing process steps impart any distinctive structural characteristics to the final product compared to the product in the prior art, the patentability of the product cited in claim 8 does not depend on its method of production.

18. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kroumpouzos et al. (J. Invest. Dermatol., 1996, 106(4): pp623), as evidenced by Chen et al. (PNAS 1998, 95: 9512-9517, IDS).

Kroumpouzos et al. teach a 65 kD membrane GPI-glycoprotein which is isolated from malignant melanoma, is overexpressed in melanoma tissues as compared to normal tissues, has diacylglycerol as a lipid structure of GPI anchor and is sensitive to phospholipase PI-PLC. Because the protein of Kroumpouzos et al. is sensitive to PI-PLC, its GPI-anchor would have a non-acetylated inositol ring as evidenced by Chen et al. Chen et al. teach that the PI-PLC resistance of a GPI-anchored protein is due to acetylation of an inositol hydroxyl group (see page 9512, left column, last paragraph).

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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12/7/07